FG

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Applicants	:	Nobuyuki Itoh et al.
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For	:	HUMAN FGF-23 GENE AND GENE EXPRESSION PRODUCTS
Examiner	:	
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FILING FORMAL DRAWINGS

Commissioner for Patents:

Enclosed are 22 sheets of formal drawings, Figures 1-16, for filing in the above-identified application.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC

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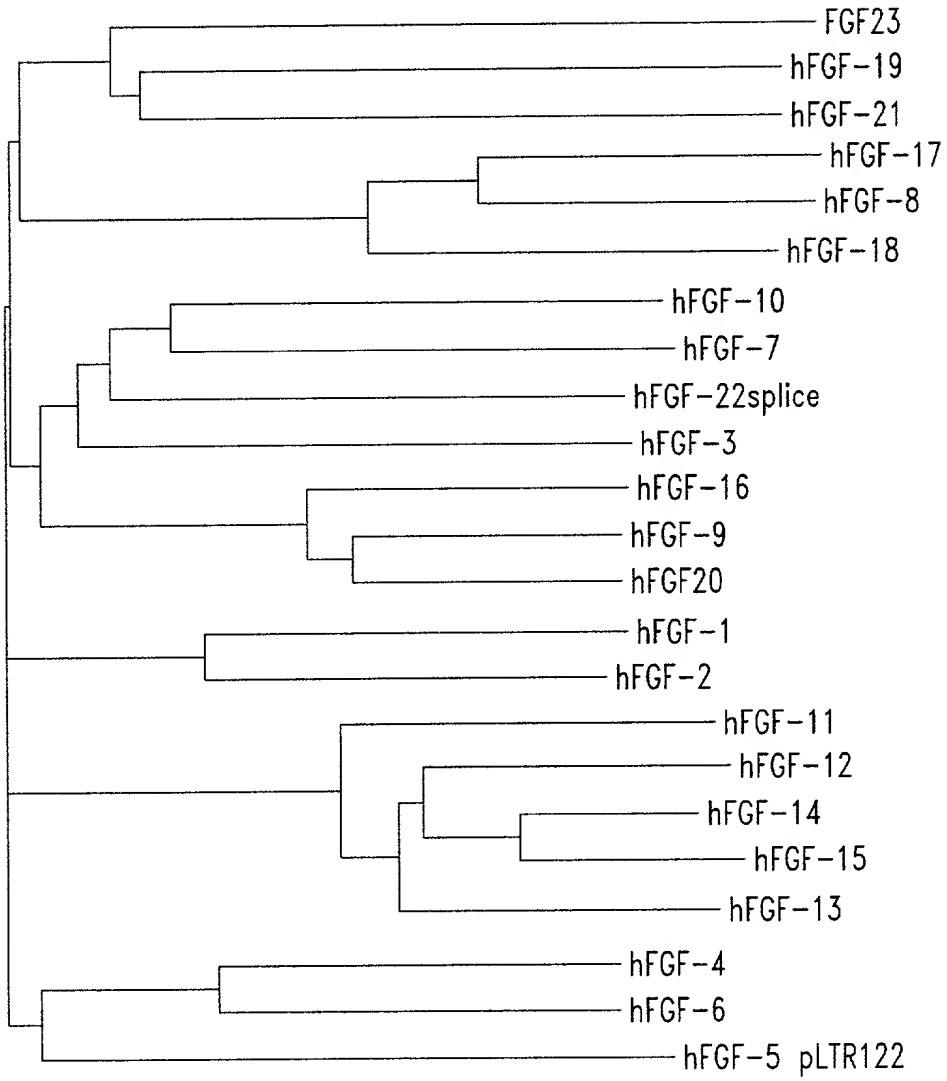
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Fig. 1

Mouse FGF-23

```
        10        20        30        40        50        60
ATGCTAGGGACCTGCCTTAGACTCCTGGTGGGCGTGCTCTGCACTGTCTGCAGCTTGGGC
M  L  G  T  C  L  R  L  L  V  G  V  L  C  T  V  C  S  L  G

        70        80        90       100       110       120
ACTGCTAGAGCCTATCCAGACACTTCCCCATTGCTTGGCTCCAACTGGGGAAGCCTGACC
T  A  R  A  Y  P  D  T  S  P  L  L  G  S  N  W  G  S  L  T

       130       140       150       160       170       180
CACCTGTACACGGCTACAGCCAGGACCAGCTATCACCTACAGATCCATAGGGATGGTCAT
H  L  Y  T  A  T  A  R  T  S  Y  H  L  Q  I  H  R  D  G  H

       190       200       210       220       230       240
GTAGATGGCACCCCCCATCAGACCATCTACAGTGCCCTGATGATTACATCAGAGGACGCC
V  D  G  T  P  H  Q  T  I  Y  S  A  L  M  I  T  S  E  D  A

       250       260       270       280       290       300
GGCTCTGTGGTGATAACAGGAGCCATGACTCGAAGGTTCCTTTGTATGGATCTCCACGGC
G  S  V  V  I  T  G  A  M  T  R  R  F  L  C  M  D  L  H  G

       310       320       330       340       350       360
AACATTTTTGGATCGCTTCACTTCAGCCCAGAGAATTGCAAGTTCCGCCAGTGGACGCTG
N  I  F  G  S  L  H  F  S  P  E  N  C  K  F  R  Q  W  T  L

       370       380       390       400       410       420
GAGAATGGCTATGACGTCTACTTGTCGCAGAAGCATCACTACCTGGTGAGCCTGGGCCGC
E  N  G  Y  D  V  Y  L  S  Q  K  H  H  Y  L  V  S  L  G  R

       430       440       450       460       470       480
GCCAAGCGCATTTTCCAGCCGGGCACCAACCCGCCGCCCTTCTCCCAGTTCCTGGCTCGC
A  K  R  I  F  Q  P  G  T  N  P  P  P  F  S  Q  F  L  A  R

       490       500       510       520       530       540
AGGAACGAGGTCCCGCTGCTGCACTTCTACACTGTTCGCCCACGGCGCCACACGCGCAGC
R  N  E  V  P  L  L  H  F  Y  T  V  R  P  R  R  H  T  R  S

       550       560       570       580       590       600
GCCGAGGACCCACCCGAGCGCGACCCACTGAACGTGCTCAAGCCGCGGCCCCGCGCCACG
A  E  D  P  P  E  R  D  P  L  N  V  L  K  P  R  P  R  A  T
```

Fig. 2A

```
          550         560         570         580         590         600
GCCGAGGACCCACCCGAGCGCGACCCACTGAACGTGCTCAAGCCGCGGCCCCGCGCCACG
A  E  D  P  P  E  R  D  P  L  N  V  L  K  P  R  P  R  A  T

          610         620         630         640         650         660
CCTGTGCCTGTATCCTGCTCTCGCGAGCTGCCGAGCGCAGAGGAAGGTGGCCCCGCAGCC
P  V  P  V  S  C  S  R  E  L  P  S  A  E  E  G  G  P  A  A

          670         680         690         700         710         720
AGCGATCCTCTGGGGGTGCTGCGCAGAGGCCGTGGAGATGCTCGCGGGGGCGCGGGAGGC
S  D  P  L  G  V  L  R  R  G  R  G  D  A  R  G  G  A  G  G

          730         740         750         760
GCGGATAGGTGTCGCCCCTTTCCCAGGTTCGTCTAG
A  D  R  C  R  P  F  P  R  F  V  *
```

Fig. 2B

Human FGF-23

```
        10        20        30        40        50        60
atgttgggggcccgcctcaggctctgggtctgtgccttgtgcagcgtctgcagcatgagc
M  L  G  A  R  L  R  L  W  V  C  A  L  C  S  V  C  S  M  S

        70        80        90       100       110       120
gtcctcagagcctatcccaatgcctccccactgctcggctccagctggggtggcctgatc
V  L  R  A  Y  P  N  A  S  P  L  L  G  S  S  W  G  G  L  I

       130       140       150       160       170       180
cacctgtacacagccacagccaggaacagctaccacctgcagatccacaagaatggccat
H  L  Y  T  A  T  A  R  N  S  Y  H  L  Q  I  H  K  N  G  H

       190       200       210       220       230       240
gtggatggcgcaccccatcagaccatctacagtgccctgatgatcagatcagaggatgct
V  D  G  A  P  H  Q  T  I  Y  S  A  L  M  I  R  S  E  D  A

       250       260       270       280       290       300
ggctttgtggtgattacaggtgtgatgagcagaagatacctctgcatggatttcagaggc
G  F  V  V  I  T  G  V  M  S  R  R  Y  L  C  M  D  F  R  G

       310       320       330       340       350       360
aacatttttggatcacactatttcgacccggagaactgcaggttccaacaccagacgctg
N  I  F  G  S  H  Y  F  D  P  E  N  C  R  F  Q  H  Q  T  L

       370       380       390       400       410       420
gaaaacgggtacgacgtctaccactctcctcagtatcacttcctggtcagtctgggccgg
E  N  G  Y  D  V  Y  H  S  P  Q  Y  H  F  L  V  S  L  G  R

       430       440       450       460       470       480
gcgaagagagccttcctgccaggcatgaacccacccccgtactcccagttcctgtcccgg
A  K  R  A  F  L  P  G  M  N  P  P  P  Y  S  Q  F  L  S  R

       490       500       510       520       530       540
aggaacgagatcccccctaattcacttcaacacccccataccacggcggcacacccggagc
R  N  E  I  P  L  I  H  F  N  T  P  I  P  R  R  H  T  R  S

       550       560       570       580       590       600
gccgaggacgactcggagcgggacccccctgaacgtgctgaagccccgggcccggatgacc
A  E  D  D  S  E  R  D  P  L  N  V  L  K  P  R  A  R  M  T
```

Fig. 3A

```
       610        620        630        640        650        660
ccggccccggcctcctgttcacaggagctcccgagcgccgaggacaacagcccgatggcc
P  A  P  A  S  C  S  Q  E  L  P  S  A  E  D  N  S  P  M  A

       670        680        690        700        710        720
agtgacccattaggggtggtcaggggcggtcgagtgaacacgcacgctgggggaacgggc
S  D  P  L  G  V  V  R  G  G  R  V  N  T  H  A  G  G  T  G

       730        740        750        760
ccggaaggctgccgccccttcgccaagttcatctag
P  E  G  C  R  P  F  A  K  F  I  *
```


Fig. 3B

```
Mouse FGF-23    MLGTCLRLLVGVLCTVCSLGTARAYPDTSPLLGSNWGSLTHLYTATARTSYHLQIHRDGH  60
                ***. *** * .**.***... ****..****** .**.*.******** .******* ..**
Human FGF-23    MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSSWGGLIHLYTATARNSYHLQIHKNGH  60

                VDGTPHQTIYSALMITSEDAGSVVITGAMTRRFLCMDLHGNIFGSLHFSPENCKFRQWTL  120
                ***.*********** ***** *****.*.**.****..****** .*.****.*.. **
                VDGAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENCRFQHQTL  120

                ENGYDVYLSQKHHYLVSLGRAKRIFQPGTNPPPFSQFLARRNEVPLLHFYTVRPRRHTRS  180
                ******* *...*.********* * ** ****.****.****.**.** *  *******
                ENGYDVYHSPQYHFLVSLGRAKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTPIPRRHTRS  180

                AEDPPERDPLNVLKPRPRATPVPVSCSRELPSAEEGGPAASDPLGVLRRGRGDARGGAGG  240
                *** .*********.* **.*.***.******...* *******.* **  ....*..*
                AEDDSERDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTG  240

                ADRCRPFPRFV  251
                .. ****..*.
                PEGCRPFAKFI  251
```

Fig. 4

```
Human FGF-23    MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSSWGG---LIHLYTATAR--NSYHL   53
                   ...*. *   .   .   *...*.*  .  .**.  * ****.... .*. *
Human FGF-19    MRSGCVVVHVWILAGLWLAVAGRPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFL   60

                QIHKNGHVDGAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENC  113
                .*. .* ** *. *. .* * *.. .   *.*.** * *****. *.. *   .. *.*
                RIRADGVVDCARGQSAHSLLEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDC  120

                RFQHQTLENGYDVYHSPQYHFLVSLGRAK-RAFLPGMNPPPYSQFLSRRNEIPLIHFNTP  172
                *....  .**.**.* .... ***..** *..  ...  * *.**..  .*
                AFEEEIRPDGYNVYRSEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLR  180

                IPRRHTRSAEDDSERDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRV  232

                GHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK                          216

                NTHAGGTGPEGCRPFAKFI                                            251
```

Fig. 5

```
Human FGF-23        MLGARLRLWVCALCS-VCSMSVLRAYPNASPLLG-SSWGGLIHLYTATARNS-YH   52
                    ***..*.....*..****  ..     .***..*...  *
Human FGF-21    MDSDETGFEHSGLWVSVLAGLLLGACQAHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAH   60

                LQIHKNGHVDGAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPEN  112
                *.*...* *.**..*.  * * ... ..*. * ** ...*.**   *...** .****.
                LEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEA  120

                CRFQHQTLENGYDVYHSPQYHFLVSLGRAKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTP  172
                *.*..  **.**.**.*.... * .*.. .. .*. ..**. .. * .. .*
                CSFRELLLEDGYNVYQSEAHGLPLHLPGNKSP-HRDPAPRGPARFLPLPGLPPALP--EP  177

                IPRRHTRSAEDDSERDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRV  232
                 *   .. . * ...***... *.. ..*.
                -PGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS                            209

                NTHAGGTGPEGCRPFAKFI                                          251
```

Fig. 6

Codon usage for yeast (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
Gly	GGG	33.00	0.86	0.01
Gly	GGA	70.00	1.82	0.02
Gly	GGT	2672.00	69.62	0.91
Gly	GGC	171.00	4.46	0.06
Glu	GAG	277.00	7.22	0.10
Glu	GAA	2442.00	63.63	0.90
Asp	GAT	1100.00	28.66	0.48
Asp	GAC	1211.00	31.55	0.52
Val	GTG	117.00	3.05	0.04
Val	GTA	75.00	1.95	0.03
Val	GTT	1548.00	40.33	0.56
Val	GTC	1026.00	26.73	0.37
Ala	GCG	36.00	0.94	0.01
Ala	GCA	203.00	5.29	0.06
Ala	GCT	2221.00	57.87	0.65
Ala	GCC	969.00	25.25	0.28
Arg	AGG	20.00	0.52	0.01
Arg	AGA	1336.00	34.81	0.83
Ser	AGT	116.00	3.02	0.05
Ser	AGC	94.00	2.45	0.04
Lys	AAG	2365.00	61.62	0.78
Lys	AAA	651.00	16.96	0.22
Asn	AAT	347.00	9.04	0.22
Asn	AAC	1259.00	32.80	0.78
Met	ATG	766.00	19.96	1.00
Ile	ATA	43.00	1.12	0.02
Ile	ATT	1223.00	31.87	0.52
Ile	ATC	1070.00	27.88	0.46
Thr	ACG	28.00	0.73	0.01
Thr	ACA	126.00	3.28	0.06

Fig. 7A

Thr	ACT	1129.00	29.42	0.50
Thr	ACC	962.00	25.07	0.43
Trp	TGG	325.00	8.47	1.00
End	TGA	10.00	0.26	0.09
Cys	TGT	254.00	6.62	0.89
Cys	TGC	33.00	0.86	0.11
End	TAG	11.00	0.29	0.10
End	TAA	85.00	2.21	0.80
Tyr	TAT	219.00	5.71	0.19
Tyr	TAC	913.00	23.79	0.81
Leu	TTG	2202.00	57.38	0.69
Leu	TTA	576.00	15.01	0.18
Phe	TTT	432.00	11.26	0.27
Phe	TTC	1145.00	29.83	0.73
Ser	TCG	26.00	0.68	0.01
Ser	TCA	149.00	3.88	0.06
Ser	TCT	1279.00	33.33	0.52
Ser	TCC	818.00	21.31	0.33
Arg	CGG	0.00	0.00	0.00
Arg	CGA	1.00	0.03	0.00
Arg	CGT	249.00	6.49	0.15
Arg	CGC	5.00	0.13	0.00
Gln	CAG	62.00	1.62	0.05
Gln	CAA	1225.00	31.92	0.95
His	CAT	236.00	6.15	0.35
His	CAC	433.00	11.28	0.65
Leu	CTG	52.00	1.35	0.02
Leu	CTA	236.00	6.15	0.07
Leu	CTT	90.00	2.35	0.03
Leu	CTC	14.00	0.36	0.00
Pro	CCG	10.00	0.26	0.01
Pro	CCA	1271.00	33.12	0.80
Pro	CCT	279.00	7.27	0.18
Pro	CCC	33.00	0.86	0.02

Fig. 7B

Codon usage for Drosophila (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
Gly	GGG	6.00	0.28	0.00
Gly	GGA	380.00	18.04	0.22
Gly	GGT	575.00	27.29	0.34
Gly	GGC	746.00	35.41	0.44
Glu	GAG	1217.00	57.77	0.91
Glu	GAA	115.00	5.46	0.09
Asp	GAT	503.00	23.88	0.43
Asp	GAC	654.00	31.04	0.57
Val	GTG	719.00	34.13	0.45
Val	GTA	29.00	1.38	0.02
Val	GTT	226.00	10.73	0.14
Val	GTC	608.00	28.86	0.38
Ala	GCG	94.00	4.46	0.05
Ala	GCA	80.00	3.80	0.04
Ala	GCT	446.00	21.17	0.24
Ala	GCC	1277.00	60.61	0.67
Arg	AGG	48.00	2.28	0.06
Arg	AGA	12.00	0.57	0.01
Ser	AGT	16.00	0.76	0.01
Ser	AGC	267.00	12.67	0.23
Lys	AAG	1360.00	64.55	0.93
Lys	AAA	108.00	5.13	0.07
Asn	AAT	127.00	6.03	0.13
Asn	AAC	878.00	41.67	0.87
Met	ATG	387.00	18.37	1.00
Ile	ATA	4.00	0.19	0.00
Ile	ATT	390.00	18.51	0.29
Ile	ATC	969.00	45.99	0.71
Thr	ACG	114.00	5.41	0.08
Thr	ACA	34.00	1.61	0.02

Fig. 8A

Thr	ACT	164.00	7.78	0.11
Thr	ACC	1127.00	53.49	0.78
Trp	TGG	243.00	11.53	1.00
End	TGA	1.00	0.05	0.01
Cys	TGT	20.00	0.95	0.08
Cys	TGC	220.00	10.44	0.92
End	TAG	12.00	0.57	0.17
End	TAA	58.00	2.75	0.82
Tyr	TAT	113.00	5.36	0.16
Tyr	TAC	574.00	27.25	0.84
Leu	TTG	210.00	9.97	0.12
Leu	TTA	9.00	0.43	0.01
Phe	TTT	62.00	2.94	0.09
Phe	TTC	635.00	30.14	0.91
Ser	TCG	195.00	9.26	0.17
Ser	TCA	29.00	1.38	0.02
Ser	TCT	103.00	4.89	0.09
Ser	TCC	558.00	26.49	0.48
Arg	CGG	7.00	0.33	0.01
Arg	CGA	25.00	1.19	0.03
Arg	CGT	281.00	13.34	0.34
Arg	CGC	465.00	22.07	0.55
Gln	CAG	703.00	33.37	0.91
Gln	CAA	66.00	3.13	0.09
His	CAT	88.00	4.18	0.22
His	CAC	312.00	14.81	0.78
Leu	CTG	1182.00	56.10	0.69
Leu	CTA	21.00	1.00	0.01
Leu	CTT	55.00	2.61	0.03
Leu	CTC	224.00	10.63	0.13
Pro	CCG	84.00	3.99	0.09
Pro	CCA	135.00	6.41	0.15
Pro	CCT	72.00	3.42	0.08
Pro	CCC	626.00	29.71	0.68

Fig. 8B

Codon usage for enteric bacterial (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
Gly	GGG	13.00	1.89	0.02
Gly	GGA	3.00	0.44	0.00
Gly	GGU	365.00	52.99	0.59
Gly	GGC	238.00	34.55	0.38
Glu	GAG	108.00	15.68	0.22
Glu	GAA	394.00	57.20	0.78
Asp	GAU	149.00	21.63	0.33
Asp	GAC	298.00	43.26	0.67
Val	GUG	93.00	13.50	0.16
Val	GUA	146.00	21.20	0.26
Val	GUU	289.00	41.96	0.51
Val	GUC	38.00	5.52	0.07
Ala	GCG	161.00	23.37	0.26
Ala	GCA	173.00	25.12	0.28
Ala	GCU	212.00	30.78	0.35
Ala	GCC	62.00	9.00	0.10
Arg	AGG	1.00	0.15	0.00
Arg	AGA	0.00	0.00	0.00
Ser	AGU	9.00	1.31	0.03
Ser	AGC	71.00	10.31	0.20
Lys	AAG	111.00	16.11	0.26
Lys	AAA	320.00	46.46	0.74
Asn	AAU	19.00	2.76	0.06
Asn	AAC	274.00	39.78	0.94
Met	AUG	170.00	24.68	1.00
Ile	AUA	1.00	0.15	0.00
Ile	AUU	70.00	10.16	0.17
Ile	AUC	345.00	50.09	0.83
Thr	ACG	25.00	3.63	0.07
Thr	ACA	14.00	2.03	0.04

Fig. 9A

Thr	ACU	130.00	18.87	0.35
Thr	ACC	206.00	29.91	0.55
Trp	UGG	55.00	7.98	1.00
End	UGA	0.00	0.00	0.00
Cys	UGU	22.00	3.19	0.49
Cys	UGC	23.00	3.34	0.51
End	UAG	0.00	0.00	0.00
End	UAA	0.00	0.00	0.00
Tyr	UAU	51.00	7.40	0.24
Tyr	UAC	157.00	22.79	0.75
Leu	UUG	18.00	2.61	0.03
Leu	UUA	12.00	1.74	0.02
Phe	UUU	51.00	7.40	0.24
Phe	UUC	166.00	24.10	0.76
Ser	UCG	14.00	2.03	0.04
Ser	UCA	7.00	1.02	0.02
Ser	UCU	120.00	17.42	0.34
Ser	UCC	131.00	19.02	0.37
Arg	CGG	1.00	0.15	0.00
Arg	CGA	2.00	0.29	0.01
Arg	CGU	290.00	42.10	0.74
Arg	CGC	96.00	13.94	0.25
Gln	CAG	233.00	33.83	0.86
Gln	CAA	37.00	5.37	0.14
His	CAU	18.00	2.61	0.17
His	CAC	85.00	12.34	0.83
Leu	CUG	480.00	69.69	0.83
Leu	CUA	2.00	0.29	0.00
Leu	CUU	25.00	3.63	0.04
Leu	CUC	38.00	5.52	0.07
Pro	CCG	190.00	27.58	0.77
Pro	CCA	36.00	5.23	0.15
Pro	CCU	19.00	2.76	0.08
Pro	CCC	1.00	0.15	0.00

Fig. 9B

Chromosomal localization of genes of the FGF family in human

Gene	Localization	Gene	Localization
FGF-1	5q31.3-q33.2	FGF-12	3q29-qter
FGF-2	4q26	FGF-13	X
FGF-3	11q13	FGF-14	13
FGF-4	11q13.3	(FGF-15)	
FGF-5	4q21	FGF-16	-
FGF-6	12p13	FGF-17	8p21
FGF-7	15q13-q22	FGF-18	5
FGF-8	10q25-q26	FGF-19	11q13.1
FGF-9	13q11-q12	FGF-20	8p21.3-p22
FGF-10	5p12-p13	FGF-21	19q13.1-qter
FGF-11	17	FGF-22	19p13.3
		FGF-23 □	12p13

Human FGF-15 gene has not been identified. The localization of human FGF-16 gene has not been determined.

Fig. 10

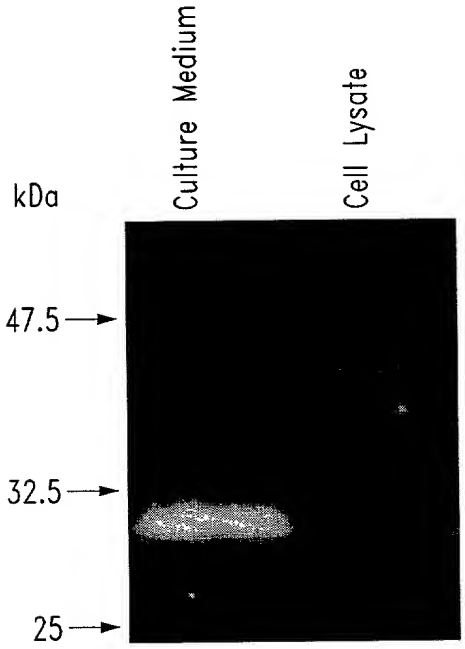


Fig. 11

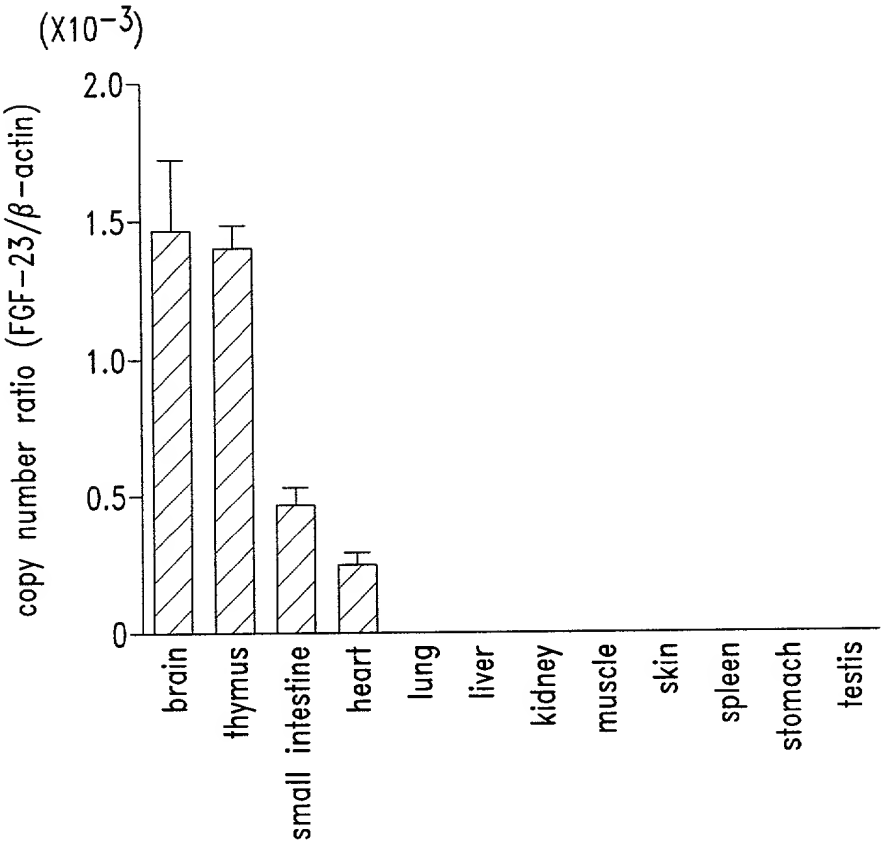

(X10^{-3})
copy number ratio (FGF-23/β-actin)
2.0
1.5
1.0
0.5
0
brain
thymus
small intestine
heart
lung
liver
kidney
muscle
skin
spleen
stomach
testis

Fig. 12

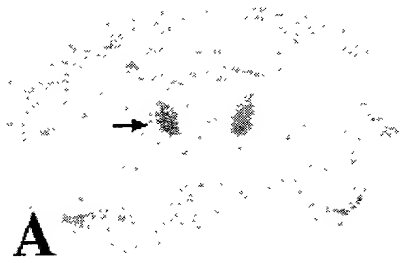


Fig. 13A

Fig. 13B

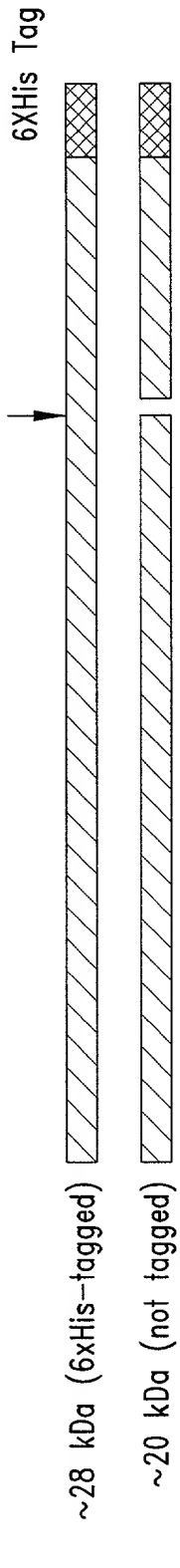

6XHis Tag
~28 kDa (6xHis-tagged)
~20 kDa (not tagged)
+~7-12 kDa (6xHis-tagged)

Fig. 14

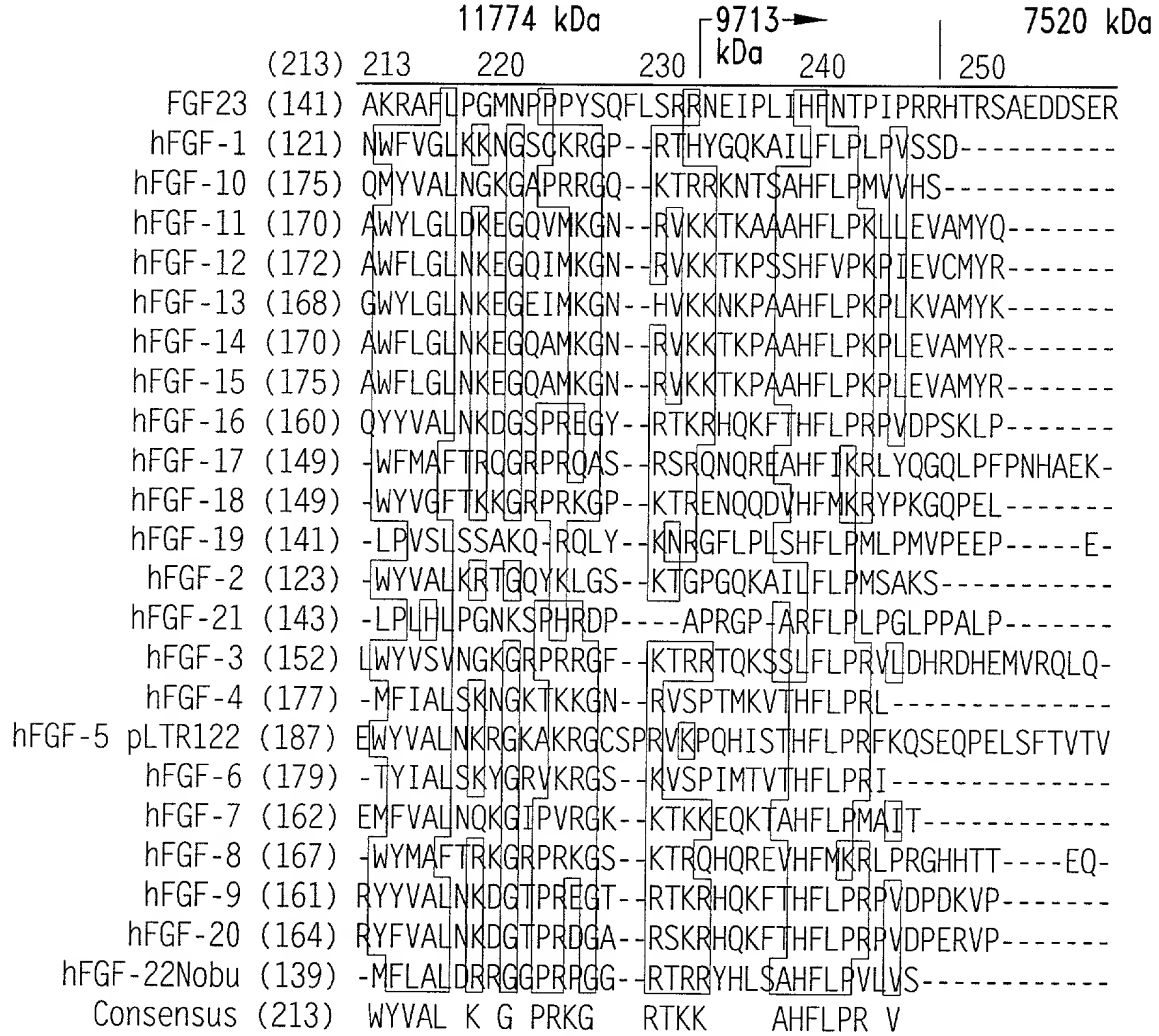
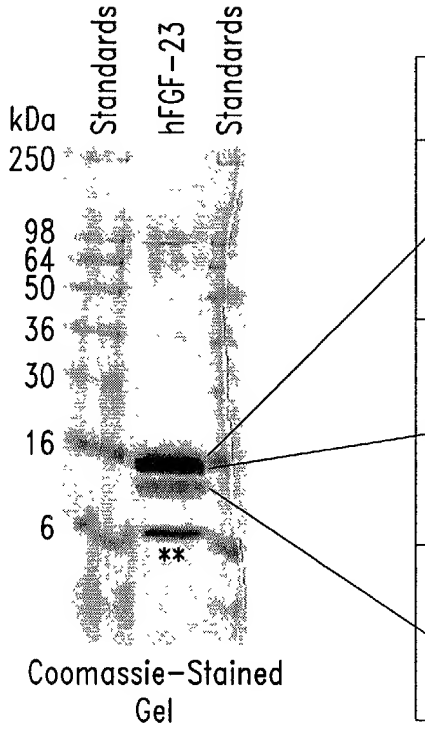

11774 kDa
9713 kDa
7520 kDa
(213) 213 220 230 240 250
FGF23 (141) AKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTPIPRRHTRSAEDDSER
hFGF-1 (121) NWFVGLKKNGSCKRGP--RTHYGQKAILFLPLPVSSD----------
hFGF-10 (175) QMYVALNGKGAPRRGQ--KTRRKNTSAHFLPMVVHS----------
hFGF-11 (170) AWYLGLDKEGQVMKGN--RVKKTKAAAHFLPKLLEVAMYQ-------
hFGF-12 (172) AWFLGLNKEGQIMKGN--RVKKTKPSSHFVPKPIEVCMYR-------
hFGF-13 (168) GWYLGLNKEGEIMKGN--HVKKNKPAAHFLPKPLKVAMYK-------
hFGF-14 (170) AWFLGLNKEGQAMKGN--RVKKTKPAAHFLPKPLEVAMYR-------
hFGF-15 (175) AWFLGLNKEGQAMKGN--RVKKTKPAAHFLPKPLEVAMYR-------
hFGF-16 (160) QYYVALNKDGSPREGY--RTKRHQKFTHFLPRPVDPSKLP-------
hFGF-17 (149) -WFMAFTRQGRPRQAS--RSRQNQREAHFIKRLYQGQLPFPNHAEK-
hFGF-18 (149) -WYVGFTKKGRPRKGP--KTRENQQDVHFMKRYPKGQPEL-------
hFGF-19 (141) -LPVSLSSAKQ-RQLY--KNRGFLPLSHFLPMLPMVPEEP-----E-
hFGF-2 (123) -WYVALKRTGQYKLGS--KTGPGQKAILFLPMSAKS----------
hFGF-21 (143) -LPLHLPGNKSPHRDP----APRGP-ARFLPLPGLPPALP-------
hFGF-3 (152) LWYVSVNGKGRPRRGF--KTRRTQKSSLFLPRVLDHRDHEMVRQLQ-
hFGF-4 (177) -MFIALSKNGKTKKGN--RVSPTMKVTHFLPRL----------
hFGF-5 pLTR122 (187) EWYVALNKRGKAKRGCSPRVKPQHISTHFLPRFKQSEQPELSFTVTV
hFGF-6 (179) -TYIALSKYGRVKRGS--KVSPIMTVTHFLPRI----------
hFGF-7 (162) EMFVALNQKGIPVRGK--KTKKEQKTAHFLPMAIT----------
hFGF-8 (167) -WYMAFTRKGRPRKGS--KTRQHQREVHFMKRLPRGHHTT----EQ-
hFGF-9 (161) RYYVALNKDGTPREGT--RTKRHQKFTHFLPRPVDPDKVP-------
hFGF-20 (164) RYFVALNKDGTPRDGA--RSKRHQKFTHFLPRPVDPERVP-------
hFGF-22Nobu (139) -MFLALDRRGGPRPGG--RTRRYHLSAHFLPVLVS----------
Consensus (213) WYVAL K G PRKG RTKK AHFLPR V

Fig. 15A

6630 kDa

```
260        270        280        290        300        310        323
DPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTGPEGCRPFAKFI
------------------------------------------------------------------
------------------------------------------------------------------
EPSLHSVPEAS-------P--SSPPAP---------------------------------------
EPSLHEIGE---KQGR-S--RKSSGTPTMNGGKVVNQDST-------------------------
EPSLHDLTEFS-RSGSGTPTKSRSVSGVLNGGKSMSHNEST-----------------------
EPSLHDVGETVPKPGV-TPSKSTSASAIMNGGKPVNKSKTT-----------------------
EPSLHDVGETVPKPGV-TPSKSTSASAIMNGGKPVNKSKTT-----------------------
SMSRDLFHYR--------------------------------------------------------
QKQFEFVGSAPTRRTKRTRR----PQPLT-------------------------------------
QKPFKYTTVTKRSRRIRPTH----PA-----------------------------------------
DLRGHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK-------------------------
------------------------------------------------------------------
EPPGILAPQPP-DVGSSDPLSMVGPSQGRSPSYAS-------------------------------
SGLPRPPGKGVQPRRRRQKQSPDNLEPSHVQASRLGSQLEASAH---------------------
------------------------------------------------------------------
PEKKKPPSPIKPKIPLSAPRKNTNSVKYRLKFRFG-------------------------------
------------------------------------------------------------------
------------------------------------------------------------------
SLRFEFLNYPPFTRSLRGSQRTWAPEPR---------------------------------------
ELYKDILSQS---------------------------------------------------------
ELYKDLLMYT---------------------------------------------------------
------------------------------------------------------------------
```

Fig. 15B



Cleavage of baculovirus-expressed 6XHis-tagged hFGF-23 secreted by Sf9 cells

N-terminal Sequence	Mass by Mass Spec	Sequence assignment	Cleavage Event(s)
NASPLLGSS	17414	N27-T178	• Signal peptide removal (P26 ↓N27) • C-terminal cleavage (R179 ↓S180) • R179 removed by contaminating carboxypeptidase
XXWGGLIHLY	16761	S34-T178	• Alternate signal peptide (G33 ↓S34) • C-terminal cleavage (R179 ↓S180) • R179 removed by contaminating carboxypeptidase
SAEDDSERDP	8204	S180-H256 (with SS bond)	• C-terminal cleavage (R179 ↓S180) • H257 removed by contaminating carboxypeptidase • Glycosylation present

** aprotinin (added to preparation)

Fig. 16